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09/363,100	07/29/99	MICKLE	D 50074/004003

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GENZYME CORPORATION C/O CLARK & ELBING
CLARK & ELBING, LLP
176 FEDERAL STREET
BOSTON MA 02110

EXAMINER	
AFREMOVA, V	
ART UNIT	PAPER NUMBER

1651

DATE MAILED:

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.

09/363,100

Applicant(s)

Mickle et al.

Examiner

Vera Afremova

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jul 23, 2001
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above, claim(s) 14-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 and 25-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 10, 13 20) ☐ Other:

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DETAILED ACTION

Claims 1-13 as amended and new claims 25-30 are under examination in the instant office action. [paper No. 12 filed 7/23/2001]. Claims 14-24 were withdrawn from further consideration pursuant to 37CFR 1.142(b) as being drawn to nonelected inventions.

Response to Arguments

Applicant's arguments filed 7/23/2001 have been fully considered but they are not persuasive for the reasons below and some arguments are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 U.S.C. § 112

Claims 1-13 as amended and new claims 25-30 are/remain rejected under 35 U.S.C. 112, *second paragraph*, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 25 are rendered indefinite by the phrase "said damaged or scarred tissues" which lacks a proper antecedent basis by omitting phrase "myocardial".

Claim 13 remains indefinite with regard to the phrase "not passaged". It is uncertain what product/composition is encompassed by this phrase. It is uncertain what composition or "cell suspension" is intended in the claimed method. Is it a cell suspension of a pure population of MSC or a bone marrow fraction containing MSC (see claims 10 and 27)? Does the phrase "non-passaged" encompasses at least one passage to separate hematopoietic cells (see specification page 11, paragraphs 2-3)? The differentiation induction of a particularly obtained cell suspension

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with MSC by 5-aza treatment appears to be critical to the present invention as disclosed (specification page 15, par. 3). Therefore, it has been stated in the prior office action that the method appeared to encompass incorporation of additional active step(s) or element(s) which is (are) omitted in the claims, such omission amounting to a gap. See MPEP § 2172.01.

Claims 3, 12, 29 and 30 remain/are indefinite and incomplete because they are not drawn to the use of active step written in active voice. The subject matter as claimed appear to belong to a preamble of the claimed method. Thus, the claimed subject matter, which is intended, might be interpreted as inherent effect rather than positive action/result.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-13 as amended and new claims 25-30 remain/are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,736,396 [A].

The claims are directed to a method for treating damaged or scarred myocardial tissue wherein the method comprises a step of administering to the damaged tissues a cellular suspension containing mesenchymal stem cells MSC. Some claims are further drawn to the use of mesenchymal cells isolated from bone marrow and to inducing differentiation of mesenchymal cells by exposing cells to 5-azacytidine at concentration of 1-100 μ M or 10 μ M. Some claims are

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further drawn to culturing the mesenchymal cells for 7 days. Some claims are further drawn to the use of MSC which were not passaged.

The cited reference is applied here as explained in the prior office action.

Applicants argued that the cited patent US 5,736,396 [A] does not clearly teach the use of a myocardial tissue as the cite of MSC administration (see response page 6). Yet, the claimed method is not particularly clear as related to a "damaged tissues" under treatment as explained above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-13 and 35-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,602,301 [IDS-10-8], Robinson et al. [U], Murry et al. [IDS-10-31] and/or WO 99/03973 [IDS-13-1] taken with Wakitani et al. [IDS-10-37] and US 5,736,396 [A].

The claims as explained above.

US 5,602,301 [IDS-10-8] teaches a method of administering skeletal myoblasts or cardiomyocytes into myocardial tissues of a living mammal (col.3, lines 41-43).

Robinson et al. [U] teach a method for treating a heart failure or injured myocardial tissue by implantation of muscle myoblasts into myocardial tissues (pages 81-82, for example).

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Murry et al. [IDS-10-31] teach a method for repairing myocardial tissues by transplanting skeletal myoblasts into damaged or injured myocardial tissues (see abstract, for example).

WO 99/03973 [IDS-13-1] discloses a method for administering to the heart tissues a cardiomyocytes producing amount of MSC (see abstract, for example).

The primary references are lacking a particular disclosure of either the use of MSC or the use of myoblasts obtained as the result of MSC differentiation for administering into myocardial or heart tissues in the method for treating damaged myocardium.

Wakitani et al. [IDS-10-37] teach myoblasts obtained from MSC by 5-aza treatment and suggests the use of treated MSC for transplantation and myogenic regeneration (see abstract). The cited reference also teaches the advantage of using MSC as a myogenic precursor over the use of myoblasts for the purpose of transplantation and surgery. The use of ex-vivo expanded and pretreated MSC is a more efficient procedure as compared to the large biopsy necessary to obtain myoblasts from autologous sites for treating a massive muscle defect. (page 1425, last par.).

The cited US 5,736,396 [A] is relied in the instant rejection for the disclosure of the use of MSC, which are derived from bone marrow and treated with 5-aza, as a composition suitable for administration in a method for treating tissues disorders, including muscle tissues.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to substitute cell compositions of the secondary references such as bone derived MSC treated with 5-aza prior to administration for the myoblast cell compositions of the primary references in the method for treating myocardial tissues of the

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primary references with a reasonable expectation of success of transplantation because the use of MSC as myogenic precursors is advantageous over myoblast compositions as taught by Wakitani et al. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC §

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (703) 308-9351. The examiner can normally be reached on Monday to Friday from 9:00 to 5:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vera Afremova,

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October 5, 2001.

SANDRA E. SAUCIER
PRIMARY EXAMINER

